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What are the indications for treatment with angiotensin-converting enzyme (ACE) inhibitors in patients with diabetes?

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EVIDENCE-BASED ANSWER

Tight control of hypertension treatment is key in preventing the vascular complications of diabetes. ACE inhibitors appear to have a protective effect that is independent of their antihypertensive effect. Unless there is a contraindication, all patients with diabetes who have hypertension should be treated with ACE inhibitors. Patients with diabetes who have microalbuminuria should be treated with ACE inhibitors, even if normotensive, as should those with overt nephropathy. (Grade of recommendation: A, based on randomized controlled trials.)

EVIDENCE SUMMARY

Several large randomized controlled trials, have demonstrated that control of hypertension in patients with diabetes prevents development or progression of nephropathy, retinopathy, and cardiovascular conditions.[1-5] On the basis of these results, the American Diabetes Association (ADA) has lowered the recommended target blood pressure in patients with diabetes to 130 over 80. ACE inhibitors are superior to calcium channel blockers (CCBs) in preventing cardiovascular outcomes in patients with diabetes.[6,7] It is not clear if this is due to beneficial effects of ACE inhibitors or adverse effects of CCBs. There is no evidence that ACE inhibitors are superior to b-blockers or diuretics in preventing cardiovascular outcomes at similar levels of blood pressure reduction.[2]

Cardiovascular disease (CVD) accounts for 60% to 75% of all deaths in patients with diabetes. Those patients with diabetes who do not have clinical evidence of CVD have a similar mortality rate from CVD as patients who do not have diabetes but do have known CVD.[8] The Heart Outcomes Prevention Evaluation (HOPE) study and the MICRO-HOPE substudy added a low dose of ramipril to the current regimen in patients with diabetes who are older than 55 years and have additional risk factors,[8] which lowered the risk of death, cardiovascular events, and nephropathy by 24% to 25% each. The cardiovascular effect was greater than that attributed to the decrease in blood pressure. It is not possible to generalize from this study the effects on risk reduction of treatment of nonhypertensive or lower-risk patients with diabetes.

ACE inhibitors also have been demonstrated to slow the progression of diabetic nephropathy in patients with type 1 diabetes[9] and may slow the progression of microalbuminuria in those with type 2 diabetes, even in the absence of hypertension.[10]

RECOMMENDATIONS FROM OTHERS

The American Association of Clinical Endocrinologists; the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure; the ADA; and Conn's Current Therapy all support ACE inhibitors in hypertensive or microalbuminuric patients with diabetes.[5,11] No published recommendations were found supporting ACE inhibitors in normotensive patients with diabetes who do not have microalbuminuria.

CLINICAL COMMENTARY

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Although the benefits from ACE inhibitors shown in the HOPE study may not be generalizable to all patients with diabetes, ACE inhibitors are so well tolerated that there is no reason (other than cost) not to use an ACE inhibitor first in patients with diabetes who have hypertension. I offer ACE inhibitors to all patients with diabetes who are older than 55 years and have an additional cardiovascular risk factor. As evidence continues to support the use of ACE inhibitors in patients with diabetes, this approach may become standard in patients who have suffered myocardial infarction and those with nondiabetic nephropathy.

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